REMARKS/ARGUMENTS

Claims 1-21, 23 are amended. Claim 22 remains unchanged.

The claim amendments address the objections of claims 8, 13, and 23. All claim amendments are supported by the specification and do not introduce new matter.

Reconsideration of the claims rejection is requested and allowance of all claims is solicited in view of the above-mentioned amendments and the arguments below.

35 USC §103 Rejection

Independent claims 1 and 23 were rejected under 35 USC §103(a) as being unpatentable over Sherman et al (US6419958) in view of Oosterbaan et al (US 6696496) and further in view of Mulye (US 2002/0155156). Claims 2-22 depend upon claim 1 and were also rejected under 35 USC §103(a) as being unpatentable over Sherman et al (US6419958) in view of Oosterbaan et al (US 6696496) and further in view of Mulye (US 2002/0155156).

The rejection of claims 1-23 is respectfully traversed because the combination of Sherman et al, with Oosterbaan et al, and with Mulye does not teach or make obvious the pharmaceutical formulation of claim 1.

A. In particular, the suggested combination does not make obvious the production of "mini-tablets of the water-soluble Venlafaxine HCL wherein each mini-tablet comprises a functional core and a functional coating layer or functional coating film, and wherein the functional core is produced with compression technology and comprises an extended release formulation of the water-soluble drug substance Venlafaxine HCl and wherein the functional coating layer or functional coating film coats the functional core and limits the initial rapid diffusion of the water-soluble drug substance from the functional core".

As was acknowledged in all the previous office actions, "Sherman does not teach the controlled release formulation of Venlafaxine HCl in the form of mini-tablets" (page 5, lines 9-11 of the office action of 4/15/10). Sherman et al teaches formulating Venlafaxine HCl in the form of spheroids because their "numerous attempts to produce extended release tablets proved to be fruitless" (see WO1999/22724, page 2, lines 20-223 and US 6,419,958 column 4, lines 58-65).

Furthermore, in WO1999/22724 and in EP0797991 (also of Sherman et al), it is also acknowledged that Venlafaxine HCl is difficult to be formulated in extended release tablets due to its **high water solubility** (572mg/ml) and several attempts to produce extended release tablets have failed, see WO1999/22724page 2, lines 15 to 25.

Oosterbaan et al (US 6696496) also does not teach how to produce mini-tablets of the extended release formulation of the water-soluble drug substance Venlafaxine HCl. The subject-matter of Oosterbaan et al (US 6696496) is limited only to low water-soluble Venlafaxine salts which have lower water-solubility (380 mg/ml or less, preferably 200 mg/ml or less, more preferably 150mg/ml) relative to Venlafaxine HCL (see column 3, lines 39-50). In other words, Oosterbaan took notice of the teachings of Sherman and deviated from using high water-soluble Venlafaxine HCl (as a person of ordinary skill would have done) and instead based his invention on the discovery of the low water soluble Venlafaxine salts (see column 2, lines 15-30, lines 56-65).

Venlafaxine salts are different compositions and have different physical (including water solubility) properties than Venlafaxine HCl. Accordingly, a person of ordinary skill cannot deduce that whatever process works for Venlafaxine salts would also work for Venlafaxine HCL, especially when there is evidence for the opposite.

Actually both Sherman and Oosterbaan teach away from producing mini-tablets of the water-soluble Venlafaxine HCL because of difficulties related to the high water solubility of Venlafaxine HCL.

Mulye (US 2002/0155156) teaches in general coating a solid dosage form of a medicament in order to produce controlled release of the active ingredient. In other words, Mulye relies in the use of a coating for producing a controlled release formulation. There is no reference in the entire specification of Mulye on how to produce mini-tablets of an extended release formulation of the water-soluble drug substance Venlafaxine HCl. Actually, nowhere, in the entire application Venlafaxine HCL is disclosed.

Accordingly, the combination of Sherman et al, with Oosterbaan et al, and with Mulye does not teach or make obvious the production of mini-tablets of the highly water soluble Venlafaxine HCL with a functional core that comprises an extended release formulation of the water-soluble drug substance Venlafaxine HCl according to claim 1. On the contrary, the suggested combination would deter a person of ordinary skill from trying to produce mini-tablets of an extended release formulation of the water-soluble drug substance Venlafaxine HCl because of the cited problems due to the high water solubility.

B. The suggested combination does not make obvious the production of mini-tablets of the highly water soluble Venlafaxine HCL, wherein "each mini-tablet comprises a functional core and a functional coating layer or functional coating film, and wherein the functional core is produced with compression technology (i.e., hydrogel) and comprises an extended release formulation of the water-soluble drug substance Venlafaxine HCl".

Sherman teaches producing spheroids of an extended release formulation of Venlafaxine HCL via extrusion and spheronization (see WO1999/22724 page 6, lines 9 to 12; page 7, lines 14 to 17; page 8, lines 6 to 11).

Oosterbaan teaches a hydrogel-based process, but the process is applied only to low water-soluble Venlafaxine salts. There is no suggestion or indication that the same hydrogel-based process would work with the high water-soluble Venlafaxine HCl.

Mulye (US 2002/0155156) teaches in general coating a solid dosage form of a medicament in order to produce controlled release of the active ingredient. There is no reference in the entire specification of Mulye on how to produce mini-tablets of the water-soluble Venlafaxine HCL with compression technology. Actually, nowhere, in the entire application Venlafaxine HCL is disclosed.

Accordingly, the combination of Sherman et al, with Oosterbaan et al, and with Mulye does not teach or make obvious the production of mini-tablets of an extended release formulation of the highly water soluble Venlafaxine HCL with compression technology. On the contrary, the suggested combination would deter a person of ordinary skill from trying to produce mini-tablets of the highly water soluble Venlafaxine HCL via compression technology.

C. The suggested combination does not make obvious the use of "a functional coating layer or functional coating film that coats the functional core and limits the initial rapid diffusion of the water-soluble drug substance from the functional core"

Shermann does not rely on a functional coating in order to produce a spheroid of an extended release formulation of Venlafaxine HCl. Furthermore, there is no reference to the need to limit the initial rapid diffusion of the water-soluble Venlafaxine HCl from the spheroids.

Oosterbaan et al also does not teach coating the Venlafaxine salt tablets with a functional coating so that that the initial rapid diffusion of the Venlafaxine HCL drug contained in the functional core would be limited.

Mulye (US 2002/0155156) teaches coating a solid dosage form of a medicament in order to produce controlled release of the active ingredient. Again, there is no reference to the need to limit the initial rapid diffusion of the water-soluble Venlafaxine HCl from a core that contains an extended formulation of the water soluble Venlafaxine HCl. Furthermore, there is no suggestion to use the disclosed coating in order to limit the

initial rapid diffusion of the Venlafaxine HCL drug contained in the functional core of a mini-tablet. Furthermore, nowhere, in the entire application Venlafaxine HCL is disclosed as being an active agent the release of which can be controlled by the disclosed coating.

Accordingly, it is concluded that the combination of Sherman et al, with Oosterbaan et al, and with Mulye does not suggest or make obvious using "a functional coating layer or functional coating film that coats the functional core and limits the initial rapid diffusion of the water-soluble drug substance from the functional core" according to claim 1

Based on the above mentioned reasons (A-C) it is concluded that the combination of Sherman et al with Oosterbaan et al and with Mulye does not teach or suggest developing a once a day extended release formulation of water-soluble Venlafaxine HCL according to claim 1. Accordingly, it is concluded that claim 1 is non-obvious and therefore patentable over the suggested combination.

Claims 2-22 depend directly or indirectly upon claim 1 and since claim 1 is non-obvious and patentable over the suggested combination, they should also be patentable over the suggested combination.

Claim 23 is a method claim corresponding to compound claim 1 and since claim 1 is patentable over the suggested combination, claim 23 should also be patentable over the suggested combination.

It is believed that all of the pending claims have been addressed in this paper. Failure to address a specific rejection, issue or comment, does not signify agreement with or concession of that rejection, issue or comment. Nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper, and the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

In view of the above, it is submitted that claims 1-23 are in condition for allowance. Reconsideration of the claims rejection is requested and allowance of all claims at an early date is solicited.

If this response is found to be incomplete, or if a telephone conference would otherwise be helpful, please call the undersigned at 781-235-4407

Respectfully submitted,

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